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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,317	07/13/2006	Frank Leenders	14836-53313	4625

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EXAMINER	
UNDERDAHL, THANE E	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,317	LEENDERS ET AL.	
	Examiner	Art Unit	
	THANE UNDERDAHL	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *8 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/21/07 has been entered.

This Office Action is in response to the Applicant's request for continued examination. Claims 1-10 are pending. Claims 8 and 9 are withdrawn. No claims are cancelled. Claims 1 has been amended. No claims are new.

Specification

The specification is objected to since it lacks a brief description of the figures.

Claim Rejections - 35 USC § 112

Claims 1-7 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The independent claim 1 includes the language "essentially consisting of". While closely related, this is not a synonym for the transitional phrase "consisting essentially of" (M.P.E.P. § 2111.03). In the interest of compact prosecution, the Examiner will read this limitation as "consisting essentially of", but clarification is required. Also claim 3 recites "preferred" enzymes, which do not precisely define the metes and bounds of the claims. It is not clear whether any other

enzyme other than that recited are part of the claimed invention. Clarification is required.

Response to Applicant's Arguments— 35 U.S.C § 103

In the response submitted by the Applicant, the 35 U.S.C § 103 (a) rejection of claims 1-5, 7 and 10 over Leskovar et al. were considered but not found persuasive.

The Applicant argues that due to the amendment to claim 1 that "any antibodies and conjugates thereof are excluded form the inventive composition", like those taught by Leskovar. Does not agree with this statement. Initially the Applicant uses the incorrect term of "essentially consisting of". While the Examiner is interpreting this phrase as "consisting essentially of", this statement is not further limiting. M.P.E.P. § 2111.03 states:

> "The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. *In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original)" and "For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., *PPG*, 156 F.3d at 1355, 48 USPQ2d at 1355"

The Examiner did not find any indication in the specification or claims what the novel and basic characteristics actually are. Until such evidence is pointed out to the Examiner, claim 1 will remained interpreted by the Examiner as "consisting of" rather than "consisting essentially of".

Also the amendment to claim 1 does not narrow that the antineoplastic agent is not modified with an antibody or conjugate. The broad term of antineoplastic agent consisting of platinum complexes and anthracyclines reads on any compound that incorporates these, including immunoconguates. While claim 5 and 6 do exclude the use of immunoconguates of these compounds by naming specific complexes these limitations are not found in claim 1.

The Applicant also argues that the synergistic effect of the claimed compounds overcomes the rejection of obviousness. The Examiner does not agree. The evidence of the secondary evidence of synergism presented by the Applicant is to a specific number of cell types using a specific enzyme namely Pseudomonas 7A glutaminase-asparaginase. These claims are far broader than the narrow examples given by the Applicant. M.P.E.P. § 716.01(b) states:

> The weight attached to evidence of secondary considerations by the examiner will depend upon its relevance to the issue of obviousness and the amount and nature of the evidence. Note the great reliance apparently placed on this type of evidence by the Supreme Court in upholding the patent in *United States v. Adams*, 383 U.S. 39,148 USPQ 479 (1966).
>
> To be given substantial weight in the determination of obviousness or nonobviousness, evidence of secondary considerations must be relevant to the subject matter as claimed, and therefore the examiner must determine whether there is a nexus between the merits of the claimed invention and the evidence of secondary considerations. *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 305 n.42, 227 USPQ 657, 673-674 n. 42 (Fed. Cir. 1985), *cert. denied*, 475 U.S. 1017 (1986). The term "nexus" designates a factually and legally sufficient connection between the objective evidence of nonobviousness and the claimed invention so that the evidence is of probative value in the determination of nonobviousness. *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 7 USPQ2d 1222 (Fed. Cir.), *cert. denied*, 488 U.S. 956 (1988)"

The claims presented by the Applicant are far broader than the examples provided and as such no Nexus exists.

Therefore the rejection stands and is repeated below with modifications to address the claim amendments.

Claims 1-5, 7 and claim 10 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Leskovar et al. (WO 89/09620 of PCT/EP89/00403). This reference is written in German. However it has a U.S. Patent Publication (US 2002/0094542) which is a 371 and as such is an English language equivalent document (see M.P.E.P., Appendix L, 35 U.S.C. 371 National stage: Commencement.) The Examiner will cite the U.S. Patent Publication for convenience, but the rejection remains over WO 89/09620.

These claims are to a combined pharmaceutical preparation comprising as active substances: (a) at least one compound having glutaminase activity (**GA**) and (b) at least one antineoplastic agent selected from platinum complexes and anthracyclines. Claim 2 limits claim 1 by teaching the compound having GA is glutaminase, glutaminase-asparaginase, glutaminase analog, derivative or modification of the same and is either of natural origin or is produced synthetically. Claim 3 limits that the compound with GA is from Pseudomonas. The Applicant is reminded that "Pseudomonas 7A glutaminase-asparaginase" is only a preferred enzyme and is not given patentable weight (see 35 U.S.C § 112 2nd rejection above) Claim 4 limit that the GA compound is modified. Claim 5 limits the type of anthracycline. Claim 7 teach the pharmaceutical preparation

further comprises a pharmaceutically acceptable carrier for oral or parenteral administration.

Leskovar et al. teach a pharmaceutical preparation that comprises the Component A which includes anthracyclines such as doxorubicin and daunomycin that have been modified by conjugating them with antibodies (paragraphs 21-23). Leskovar et al. also teach that their pharmaceutical preparation can comprise antibody immunoconjugates of the enzymes asparaginase and glutaminase (paragraph 192). Leskovar et al. does not specifically teach the addition of both the anthracyclines and glutaminase enzymes in the same composition. However Leskovar et al. does teach that antibody conjugates of xenogeneic proteins can be admixed with Component A and either administered patenterally or orally (paragraph 25-26). One of ordinary skill in the art would recognize that that a composition with active substances such as enzymes and anthracyclines would need to be mixed with a pharmaceutically acceptable carrier such as water to be administered patenterally or orally.

It would therefore have been obvious for the person of ordinary skill in the art to modify the invention of Leskovar et al. to combine an enzyme such as glutaminase with component A, which they teach as an anthracycline such as doxorubicin. Leskovar et al. provides express motivation and reasonable expectation of success by stating that "conjugates, composed of xenogeneous proteins…can be admixed to the component A" (paragraph 26).

Furthermore it would be obvious to combine the anthracycline and glutaminase since they are two components known for the same purpose (see M.P.E.P. § 2144.06).

In this case the treatment of cancer (paragraph 140 and 192). This would apply to anthracyclines that are immunoconjugated or not, since the art is replete with references that unmodified anthracyclines alone are effective against the treatment of caner

Leskovar et al. also does not teach that the compound having glutaminase activity is from *Pseudomonas*. This is a product by process claim since it defines the product as being made from a specific process or method.

However M.P.E.P. § 2113 states "product-by process claims" such as this "are not limited to the manipulations of the recited steps, only the structure implied by the steps" as cited below:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

Therefore since Leskovar et al. teaches utilizing glutaminase, it would have been obvious at the time the invention was made to use any known glutaminase (regardless of the source) with a reasonable expectation of the same success found in using the glutaminase of Leskovar. Thus it would have been *prima facie* obvious to substitute any glutaminase into the preparation of Leskovar absent any teaching of criticality for the specific enzyme claimed. Furthermore any glutaminase regardless of its source will perform the same chemical reaction and can therefore be used for the same purpose

and it would be obvious for one of ordinary skill in the art to substitute one glutaminase for the other (M.P.E.P. § 2144.06).

Therefore, the invention as a whole would have been prima facie obvious at the time of filing in view of the reference listed above and as such claims 1-5, 7 and claim 10 are not allowable.

In the response submitted by the Applicant, the 35 U.S.C § 103 (a) rejection of claims 1-7 over Leskovar et al. as applied to claim 1-5, 7 and 10 above in view of Housman et al. were considered but not found persuasive.

Concerning the remaining 35 U.S.C § 103 (a) rejections in the Office Action the Applicant argues that since the amendments of claim 1 overcome the teachings of Leskovar that they in turn overcome the remaining rejections that use this reference. However as detailed above the Examiner disagrees and believes that the combination of Lesokovar in view of Housman et al is proper and in the absence of arguments to the contrary these rejections stand for the amended claims and are repeated below.

Claim 1-7 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leskovar et al. (WO 89/09620 of PCT/EP89/00403) as applied to claim 1-5, 7 and new claim 10 above, and further in view of Housman et al. (U.S. Patent # 6,200,754, 2001).

The details of clams 1-5, 7 and 10 and their rejection are described in the above 103(a) rejection over Leskovar et al.

Claim 6 limits the pharmaceutical preparation comprising cis-platinum, oxaliplatinim or/and carboplatinum.

While Leskovar et al. teach the use of other DNA crosslinking compounds such as mitomycin C (Leskovar et al. paragraph 23) in a composition for cancer treatment he does not teach the specific use of DNA crosslinking agent cis-platinum. However Housman et al. teach that mitomycin C and cis-platinum are both DNA crosslinking agents (col 22, lines 14-15) and one of ordinary skill in the art would recognize them as common drugs for cancer treatment (col 21, line 55 to col 22, line 20). Therefore it would be obvious to replace cis-platinum or other DNA crosslinking agents such as oxaliplatinum and carboplatinum since these are art-recognized equivalents for the same purpose (M.P.E.P. § 2144.06).

Therefore, the invention as a whole would have been prima facie obvious at the time of filing in view of the references listed above and as such claims 1-7 and 10 are not allowable.

In response to this office action the applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

CONTACT INFORMATION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thane Underdahl whose telephone number is (571) 272-9042. The examiner can normally be reached Monday through Thursday, 8:00 to 17:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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